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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,145	03/23/2007	Istvan Eros	23565	9304

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EXAMINER	
LEWIS, AMY A	

ART UNIT	PAPER NUMBER
1614	

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12/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,145	EROS ET AL.	
	Examiner	Art Unit	
	Amy A. Lewis	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71-100* is/are pending in the application.

4a) Of the above claim(s) *71-79 and 87-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *80-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 7/3/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Newly submitted claim 71-100 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the application contains the following patentably distinct species (see previous office action):

1. Estrogen and progestin
1. Ondansetron
2. Terbinafine
3. Fluconazole
4. Metronidazole
5. Fenanyl
6. Nandrolone decanoate
7. Nestrone
8. Norethisterone
9. Eperisone
10. Tolperisone
11. Vinpocetine
12. Ketamine
13. Vincristine
14. Vinblastine

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Applicant previously elected progestin and estrogen in a phone call on 4/10/2008. Accordingly, claims 71-79, 87-100 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 80-86 remain under consideration as far as they read upon the elected species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5, 8, 9, 12, 13, 14, 17, 18, 20, 22, 24, 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szabo et al. (EP 509761) and Bunschoten et al. (US patent publication 2004/0192620) in view of Parab PV (US 5326566), Brynhildsen et al. (Menopause 2002) (abstract only) in further view of Pouyani et al. (US 5616568). This rejection is moot due to cancellation of the claims. However, it is **newly applied** to claims 80-86 for same reasons cited in the previous action:

Szabo et al. teaches the use of lyotropic liquid (liquid crystal gel) for a dermal preparation which assures a sufficient and uniform release of the active ingredient (pg 2, lines 29-30) (claims 1, 17 and 28). Szabo et al. also teaches the making of lyotropic liquid crystalline system by varying the quantity of the components to the particle size of the liquid crystal and the ratio of the liquid crystalline arrangement compared to the total system for ensuring uniform release corresponding to the therapeutic demands (pg 2, lines 37-41). Szabo et al. further teaches the addition of 40-70 wt. % of liquid polyoxyethylene and 10-20 wt. % of solid polyoxiethylene and 2- 20% wt. % of propylene glycol (pg 2, lines 45-50) (claims 2 and 3). Szabo et al. teaches the use of various polyoxiethylene compounds (pg 2, 53- 57) and refers to them as PEG's in their

example tables V (pg 6 and pg 7). Szabo et al. teaches the procedure to make the composition and describes the method of adding polyoxiethylene (liquid and solid) with polyethylene glycol (pg 3, lines 7-10) and then adding the active ingredient (pg 3, lines 11-12). Szabo et al. teaches the combination of polyoxyethylene and propylene glycol in the range that the applicant claims and also mentions addition of active agents to the mix. Szabo et al. uses the **polyoxyethylenes** as a polymer to make the liquid crystalline gel, hence creating the ideal environment for controlled and uniform release of the drug in a transdermal patch.

Szabo et al. does not teach the use of sodium and zinc hyaluronate salts, isopropyl myristate and specifically use of hormones as active agents.

Bunschoten et al. teaches the use of a method of contraception by administration of estrogenic component and a progestogenic component (0069) as a transdermal patch among other formats (0042) (claims 17, 18, and 26). Bunschoten et al. also teaches the use of levonogestrel, etonogestrel and gestodene (0082) (claims 20, 22, 24). Bunschoten et al. further teaches that transmucosal delivery systems include patches among others and contain excipients such as solubilizers, e.g. propylene glycol and other vehicles e.g., fatty acid esters and hydrophilic polymers such as hyaluronic acid (0092) (claims 1 and 28). Suitable penetration enhancing agents such as isopropyl myristate and propylene glycol are among others (0120) (claims 1, 17 and 28). Isopropyl myristate is used by Bunschoten et al. as a suitable penetration enhancer for the estrediol and progestin compounds in transdermal patch.

Bunschoten et al. does not teach the use of polyoxyethylene glycol trioleate and the weight ratio of isopropyl myristate.

Parab PV teaches that the mixture of isopropyl myristate (IPM) and dibutyl adipate (DBA) enhances and controls the epidermal, dermal and transdermal penetration of various topically applied pharmacological agents (column 3, lines 60-65). IPM is known as a penetration enhancer for topical application and use of a combination with DBA provides synergistic effect and devoid of side effects. Parab PV also teaches that it is novel agents that enhance and/or control epidermal and dermal absorption of dermatological agents and enhance and control delivery of systemically active therapeutic agents through skin and into the general circulation. Parab PV also mention that the pharmacological agents such as steroids specially gesterone, estradiol, progesterone along with other examples. The concentration of IPM is between the ranges of 1-30% by weight of the composition (column 7, lines 8-10) (claim 9). Parab PV also teaches the addition of propylene glycol as a penetration enhancer in example 2 and the weight is 7% of the whole composition. The weight ratio between DBA and propylene glycol is 2:1 (claim 8). Parab PV further teaches that it is suitable for a patch along with others. The teachings of Parab PV suggest that the ratio adjustment between various chemicals that enhance the penetration of the drug via a transdermal patch helps create an ideal combination.

Parab PV does not teach the use of hyaluronic acid as permeation enhancer.

Pouyani et al. teaches that hyaluronic acid (HA) degrades very soon and functionalized or crosslinked HA facilitates subsequent attachment of additional components such as bioaffecting agents including drugs (column 2, lines 50-54). Pouyani et al. further teaches that hyaluronate posses a number of characteristics that make it advantageous to be used as a drug carrier as it is biocompatible, non-immunogenic and degrades in the body by enzymes , and possesses many covalent groups that are amenable for modification (column 3, lines 60-65). HA often occurs

naturally as sodium salts (column 4, lines 8-10) (claim 12, 13 and 14). One ordinary skill in the art would substitute sodium with any other elements that are known to provide stability to hyaluronic acid. Transdermal patches would benefit from the use of stable hyaluronic acid in salt forms that enables HA to be a better drug carrier.

Brynhildsen et al. teaches the use of transdermal patch containing estradiol/norethisterone acetate to treat postmenopausal women (claim 26).

It would be prima facie obvious to combine polyoxyethylene glyceryl trioleate, isopropyl myristate, propylene glycol and hyaluronic acid in liquid crystal gel as compositions each of which is taught by the prior art to be useful for the same purpose to form a composition for a transdermal patch to be used for the very same purpose with a known bioactive component. The idea of combining them flows logically from their having been individually taught in the prior art.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." (MPEP 2144.05)

One would be motivated to make this combination of the biocompatible, permeation enhancers to deliver the bioactive drugs transdermally with low immunogenic response. Given the state of the art as evidenced by the teachings of the cited references there would have been a reasonable expectation of success in combining the teachings of the cited references to obtain a

composition of hormones that has effective pharmaceutical and therapeutic effect in the form of a transdermal patch.

Applicant alleges that the Szabo et al. reference teaches an anhydrous transdermal composition and is not equivalent to the instantly claimed invention which contains oil and aqueous phases (See Remarks p. 12). In response, Szabo et al. in fact do teach oil in water emulsions (see p. 2, lines 25-30), and still teaches the polyoxyethylene ingredients for transdermal applications.

Applicant also argue that hylauronic acid is not mentioned in the Szabo reference, thus is does not suggest using it (see Remarks p. 12-13). This is correct; however the examiner also acknowledges that the reference does NOT teach the use of sodium and zinc hyaluronate salts thus including the subsequent references.

Applicants argue that there is "no teaching from the combination of EP 0509761 B1 and BUNSCHOTEN et al to prepare a liquid crystalline gel for the transdermal administration of any pharmaceutically active ingredient" (See Remarks p. 14). In response, the Bunschoten reference and the Szabo reference are directed to transdermal delivery of pharmaceutical ingredients, with the Bunchoten reference providing motivation for delivering progestins and estrogens transdermally (see rejection recited above).

The arguments that the Szabo, Bunschoten and Parab references do not teach hyaluronic acid or it's salts (see Remarks pages 12, 14, 15, 17 and 19) is not convincing because the examiner does not allege this…and uses the teachings Pouyani et al., which state that the salt forms of HA increase the ability of HA to be a good drug carrier (see rejection statement above).

Applicant argues that the present invention does not use a transdermal path (see Remarks p. 14-15), and actually "avoid the…patch" citing to the specification. This is not persuasive because, the claims in fact recite using a transdermal composition *generally* and do not exclude such application as a path, thus art teaching a transdermal patch is in fact a species of transdermal application which meets the limitation of "transdermal composition".

Applicants argue that they "have a good argument", the allegation that the application is "new" and they have received "equivalent patents in Europe, Eurasia, and in Hungary" (See Remarks p. 16 and 23). These arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references. The U.S. Patent Office is *not* the European, Eurasian or Hungarian Patent Office, and as such has different statutes, rules, and practices: Patentability in another foreign office is not convincing of patentability here.

Applicants then go on the describe the "essence" of their invention and go on to analyze the references separately. (See Remarks p. 17-23).In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The examiner has in fact provided motivation for combining the above cited references in order to arrive at the instant invention (again, see rejection statement above).

Therefore the invention is prima facie obvious and the rejection is maintained over new claims 80-86.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy A. Lewis whose telephone number is 571-272-9032. The examiner can normally be reached on Monday-Friday 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amy A Lewis/
Examiner, Art Unit 1614

/Ardin Marschel/
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